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ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.

(54) Title: THERAPUTIC METHODS AND USES OF SAPOGENINS AND THEIR DERIVATIVES

(57) Abstract: The invention discloses therapeutic methods and uses of certain steroidal sapogenins, related compounds and deriva-
tives thereof, in the treatment of non-cognitive neurodegeneration, non-cognitive neuromuscular degeneration, motor-sensory neu-
rodegeneration or receptor dysfunction or loss in the absence of cognitive, neural and neuromuscular impairment.

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A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61K31/585 A61P9/02 A61P9/04 A61P11/06 A61P21/00
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According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

CHEM ABS Data, SCISEARCH, BIOSIS, MEDLINE, EMBASE, WPI Data, EPO-Internal, PAJ

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 1 024 146 A (INST OF RADIATION MEDICINE ACA) 2 August 2000 (2000-08-02) page 19, line 11 - line 12 page 33, line 46 -page 34, line 27 claims 1,3-20	1-7
X	WO 01 49703 A (HU YAER ;XIA ZONGQIN (CN); GUNNING PHIL (GB); HANSON JIM (GB); PHY) 12 July 2001 (2001-07-12) page 1, line 1 - line 22 page 7, line 11 -page 15, line 4 page 15, line 6 -page 16, line 24 page 22, line 32 - line 34 page 23, line 3 - line 35 claims 1-20,22,26,28,29	1-8

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *G* document member of the same patent family

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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X	<p>WO 01 23406 A (HU YAER ;XIA ZONGQIN (CN); GUNNING PHIL (GB); HANSON JIM (GB); PHY) 5 April 2001 (2001-04-05) cited in the application page 1, line 4 - line 33 page 6, line 17 -page 9, line 17 page 13, line 4 - line 23 page 13, line 28 - line 30 page 15 -page 19; table 1 claims 1-15</p> <p>---</p>	1-8
X	<p>WO 01 23408 A (HU YAER ;XIA ZONGQIN (CN); GUNNING PHIL (GB); HANSON JIM (GB); PHY) 5 April 2001 (2001-04-05) cited in the application page 1, line 4 - line 22 page 6, line 16 -page 9, line 17 page 12, line 16 - line 24 page 13, line 16 -page 14, line 27 claims 1-13</p> <p>---</p>	1-8
X	<p>DE 43 03 214 A (MARKS WOLFGANG) 11 August 1994 (1994-08-11) cited in the application page 6, line 15 - line 26 page 7, line 10 - line 15 claims 1-3,7,14</p> <p>---</p>	1-8
X	<p>SUN, HUI ET AL: "Retinal stimulates ATP hydrolysis by purified and reconstituted ABCR, the photoreceptor-specific ATP-binding cassette transporter responsible for Stargardt disease" JOURNAL OF BIOLOGICAL CHEMISTRY (1999), 274(12), 8269-8281 , XP001165795 figures 2,3,9,10 page 8280, column 2, paragraph 3</p> <p>---</p>	1-3,5,8
X	<p>US 4 680 289 A (APPLEZWEIG NORMAN) 14 July 1987 (1987-07-14) tables I,II claims 16,18,19</p> <p>---</p>	5
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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>DATABASE WPI Section Ch, Week 199343 Derwent Publications Ltd., London, GB; Class B04, AN 1993-339641 XP002157713 & JP 05 246866 A (KATO K), 24 September 1993 (1993-09-24) abstract</p> <p>---</p>	1-8
X	<p>WO 01 23407 A (HU YAER ;XIA ZONGQIN (CN); GUNNING PHIL (GB); HANSON JIM (GB); PHY) 5 April 2001 (2001-04-05) page 6, line 20 -page 8, line 32 claims 1-5,8,14</p> <p>---</p>	1,2,5-8
X	<p>PATENT ABSTRACTS OF JAPAN vol. 2002, no. 05, 3 May 2002 (2002-05-03) & JP 2002 030096 A (KYORIN PHARMACEUT CO LTD), 29 January 2002 (2002-01-29) abstract</p> <p>---</p>	1,2,5-8
A	<p>PATENT ABSTRACTS OF JAPAN vol. 1997, no. 05, 30 May 1997 (1997-05-30) & JP 09 002957 A (MITSUBISHI CHEM CORP), 7 January 1997 (1997-01-07) abstract</p> <p>---</p>	1-8
A	<p>PATENT ABSTRACTS OF JAPAN vol. 1997, no. 05, 30 May 1997 (1997-05-30) & JP 09 002956 A (MITSUBISHI CHEM CORP), 7 January 1997 (1997-01-07) abstract</p> <p>---</p>	1-8
A	<p>WO 98 02450 A (INFLAZYME PHARMACEUTICALS LTD) 22 January 1998 (1998-01-22) example 25 page 178, line 9 - line 10 claims 27,29</p> <p>---</p>	1-8
A	<p>EP 0 659 762 A (MITSUBISHI CHEM CORP) 28 June 1995 (1995-06-28) page 108, line 23 - line 36 claims 1,3,27</p> <p>---</p>	1-8
A	<p>INOUE K ET AL: "Cholesterol induces apoptosis of cerebellar neuronal cells." BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS. UNITED STATES 5 MAR 1999, vol. 256, no. 1, 5 March 1999 (1999-03-05), pages 198-203, XP001188107 ISSN: 0006-291X the whole document</p> <p>---</p>	1-8
	<p>---</p> <p>---/---</p>	

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	KYOUNG SOOK KIM, ET AL.: "Effects of cholestanol feeding on corneal dystrophy in mice." BIOCHIMICA ET BIOPHYSICA ACTA, vol. 1085, 1991, pages 343-349, XP008027217 the whole document	1-8
X	EP 0 162 330 A (ROECAR HOLDINGS NV) 27 November 1985 (1985-11-27) page 5, paragraph 2 - paragraph 3 claim 3	1,2,4-8
E	WO 03 077869 A (SAMARITAN PHARMACEUTICALS INC ;UNIV GEORGETOWN (US)) 25 September 2003 (2003-09-25) figure 1 page 5, line 14 - line 21 claims 1-8,10-14	1,2,4-8

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
Although claims 1-8 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☒ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this International application, as follows:

see additional sheet

1. ☒ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☒ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Present claims 1-8 relate to a large number of undefined compounds in terms of "derivative" (claims 1-8) and "prodrug" (1-3 and 5-8). In fact, the claims contain so many options that a lack of clarity (and/or conciseness) within the meaning of Article 6 PCT arises to such an extent as to render a meaningful search of the claims impossible. Furthermore, present claim 1-7 relate to the treatment of a disease which actually is not well defined.

The use of the definition "non-cognitive neurodegeneration", "non-cognitive neuromuscular degeneration" or "motor-sensory neurodegeneration" or "receptor dysfunction or loss in the absence of cognitive, neural and neuromuscular impairment" in the present context is considered to lead to a lack of clarity within the meaning of Article 6 PCT. It is not fully possible to determine the diseases for which protection might legitimately be sought. The lack of clarity is such as to render a meaningful complete search over the whole scope of the claims impossible.

Consequently, the search has been carried out for those parts of the application which do appear to be clear and concise, namely the use of the compounds according to formula (I), (II), (IV) and sapogenins and saponins in relation to the treatment of diseases as specifically mentioned in claim 8.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1-2 (partially), 3, 4-8 (partially)

The use of compounds according to formula (I) and (Ia) for the manufacture of a medicament for the treatment of non-cognitive neurodegeneration, non-cognitive neuromuscular degeneration, motor-sensory neurodegeneration or receptor dysfunction or loss in the absence of cognitive, neural and neuromuscular impairment. The use of said compounds as active ingredients present in foodstuffs, food supplement and beverages.

2. Claims: 1-2 (partially) and 5-8 (partially)

The use of compounds according to formula (II) for the manufacture of a medicament for the treatment of non-cognitive neurodegeneration, non-cognitive neuromuscular degeneration, motor-sensory neurodegeneration or receptor dysfunction or loss in the absence of cognitive, neural and neuromuscular impairment. The use of said compounds as active ingredients present in foodstuffs, food supplement and beverages.

3. Claims: 1-2 (partially) and 5-8 (partially)

The use of compounds according to formula (III) for the manufacture of a medicament for the treatment of non-cognitive neurodegeneration, non-cognitive neuromuscular degeneration, motor-sensory neurodegeneration or receptor dysfunction or loss in the absence of cognitive, neural and neuromuscular impairment. The use of said compounds as active ingredients present in foodstuffs, food supplement and beverages.

4. Claims: 1-2 (partially) and 4-8 (partially).

The use of sapogenin derivatives bearing at least one X radical substituent wherein X is chosen from an halo atom, (Me-S-), (Me-SO-), (Me-SO₂-), N₃-, Nh₂-, Me-SO₂-NH-, and alkyl (i.e. compounds according to D. of claim 1) for the manufacture of a medicament for the treatment of non-cognitive neurodegeneration, non-cognitive neuromuscular degeneration, motor-sensory neurodegeneration or receptor dysfunction or loss in the absence of cognitive, neural and neuromuscular impairment, as far as not comprised by subjects 1 to 3. The use of said compounds as active ingredients present in foodstuffs, food supplement and beverages.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

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